

IN THE SPECIFICATION

Please replace the Sequence Listing with the enclosed paper copy of the substitute Sequence Listing found on the page following the Abstract.

Please amend the paragraph beginning at line 16 on page 5 as follows:

Figure 5 depicts the mobilization of *Mos1* in *C. elegans* somatic cells. (A) Engineering of the *Mos* transposase encoding sequence. Depicted therein are nucleotides 1-21 (SEQ ID NO:24), 262-279 (SEQ ID NO:25), and 1039-1058 (SEQ ID NO: 26) of the *Mos1* gene (~~SEQ ID NO: 24~~). Also depicted are the corresponding amino acids 1-4 (SEQ ID NO:27), 85-90 (SEQ ID NO:28), and 344-345 of the *Mos1* protein sequence (~~SEQ ID NO: 25~~). Restriction sites were generated at the 5' and 3' ends of the coding sequence (new sequence is indicated under the original sequence). The endogenous polyadenylation signal (boxed) was disrupted and an artificial intron (SEQ ID NO:18) was introduced in the coding sequence in order to improve transposase expression. See A. Fire, S. W. Harrison, D. Dixon, *Gene* **93**, 189 (1990). (B) Localization of *Mos1* insertions into *unc-49* and *gpa-2* genes after induction of *Mos* transposase expression in somatic cells. Open triangles: insertion sites; black rectangles: coding exons; white rectangle: non coding exonic sequence. Arrows: genomic primers used to amplify the insertions. (C) Sequence comparison of 22 insertion sites. Insertion sites are oriented relative to the 5' end of the *Mos1* transposon. Sequences that flank *Mos1* at the right end were identified by PCR. DNA purification and PCR were performed as described in H. G. van Luenen, S. D. Colloms, R. H. Plasterk, *Embo J.* **12**, 2513 (1993). The primers in *Mos1* were oJL88 (5'-CGCATGCGGCTTACTCAC (SEQ ID NO: 4)) first PCR; and oJL89 (5'-GGCCCCATCCGATTACCACCTA (SEQ ID NO: 5)) second PCR. Primers in *unc-49* were oJL19 (5'-GCGAAACGCATACCAACTGTA (SEQ ID NO: 6)) first PCR; and oJL20 (5'-TTCATGCCGAAAAGCAGGCGT (SEQ ID NO: 7)) second PCR. Primers in *gpa-2* were the same as described in H. G. van Luenen, S. D. Colloms, R. H. Plasterk, *Embo J.* **12**, 2513 (1993). PCR products were gel-purified and sequenced using oJL89 (SEQ ID NO: 5) as a primer. (positive positions on the graph), sequences that flank the left end of *Mos1* were deduced from *unc-49* and *gpa-2* sequences (negative positions on the graph).

Please amend the paragraph beginning at line 21 on page 6 as follows:

Figure 7 shows *Mos1* genomic insertions. (A) Southern blot probed with labeled *Mos1* DNA. Lane 1 to 8, strains in which insertions were detected by PCR; insertions derived from an extrachromosomal array and *Mos* transposase expressed under the heat-shock promoter. *Mos1* presence was assessed by PCR using two primers located in the transposon (oJL102 (SEQ ID NO: 1) and oJL103 (SEQ ID NO: 3)). The absence of *D. mauritiana* flanking sequence was checked using oJL102 (SEQ ID NO: 1) and oJL104 (SEQ ID NO: 2), while a PCR positive control was performed on each DNA sample using oligonucleotides located in the *cha-1* gene. The control lane is lin-15(n765) which had been used to build transgenic lines. Each lane contains 2 mg of Bgl II digested genomic DNA. The *Mos1* probe (encompassing bases 1 to 173 of the transposon) was synthesized by PCR using the pBluescriptM13+/Mos1 plasmid as a template. (B) Distribution of *Mos1* inserts on the physical map of the *C. elegans* genome. Black triangles: insertions from an extrachromosomal array. Open triangles: insertions from the integrated array oxIs25. Open circle: position of oxIs25, the integrated array of *Mos1* transposons. (C) DNA sequence of *Mos1* de novo insertions oxTi1 through oxTi6, oxTi8, oxTi9, and oxTi11 (SEQ ID NOS: 26-34 respectively) (SEQ ID NOS:29-46). Genomic fragments that flank the transposon left end were isolated by inverse PCR and sequenced. A primer was designed in the genomic region to the right of the insert and used with a *Mos1* specific primer to amplify and sequence the right end flanking the fragment. At insertion sites TA dinucleotides (bold) were duplicated during the process of transposon integration. Lower case: *Mos1* sequence. Upper case: genomic sequence. Ellipses: omitted sequence.

Please amend the paragraph beginning at line 19 on page 11 as follows:

In certain preferred embodiments, *Mos1*, a *mariner*-like transposon isolated from *Drosophila mauritiana*, is used ~~(the nucleotide and protein sequences of *Mos1* are provided as SEQ ID NOS: 24 and 25 respectively)~~. M. Medhora et al., *Genetics* **128**:311-318 (1991). See generally D. L. Hartl et al., *Annu. Rev. Genet.* **31**:337-358 (1997). *Mos1* is a member of the *mariner/Tc1* family and was initially identified in the fruitfly *Drosophila mauritiana*. J. W. Jacobson, M. M. Medhora, D. L. Hartl, *Proc. Natl. Acad. Sci. USA* **83**, 8684 (1986). Like the

other members of the *mariner/Tc1* family, *Mos1* contains a single open reading frame which encodes the transposase. The transposase binds to and cleaves at the inverted terminal repeats (ITRs) present at each end of the transposon. See, e.g. D. L. Hartl, A.R. Lohe, E. R. Lozovskaya, *Annu. Rev. Genet.* **31**, 337 (1997); R. H. Plasterk, Z. Izsvak, Z. Ivics, *Trends Genet.* **15**, 326 (1999). The *Mos1* transposase is the only protein necessary for transposition *in vitro*. L. R. Tosi, S. M. Beverly, *Nucleic Acids Res.* **28**, 784 (2000). Because no additional factors are required for transposition, the *Mos1* transposon should be capable of transposition in heterologous species, and indeed the transposon has been mobilized in species evolutionarily distant from *Drosophila*. F. J. Gueiros-Filho, S. M. Beverly, *Science* **276**, 1716 (1997); J. M. Fadool, D. L. Hartl, J. E. Dowling, *Proc. Natl. Acad. Sci. USA* **95**, 5182 (1998); A Sherman, et al., *Nat. Biotechnol.* **16**, 1050 (1998); C. J. Coates, N. Jasinskeine, L. Miyashiro, A. A. James, *Proc. Natl. Acad. Sci. USA* **95**, 3748 (1998).

Please amend the paragraph beginning at line 20 on page 32 as follows:

CTCTTTTCCAGACGAGTAccaggtgtac.....tacacctgaTATATCCTTTTG TTCCTT (SEQ ID NOS: 35
47 and 48)

CTCTTTTCCAGACGAGTA-----TATATCCTTTTG TTCCTT (SEQ ID NO: 36 49)

CTCTTTTCCAGACGAGTA-----aTATATCCTTTTG TTCCTT (SEQ ID NO: 37 50)

CTCTTTTCCAGACGAGTA-----tgaTATATCCTTTTG TTCCTT (SEQ ID NO: 38 51)

CTCTTTTCCAGACGAGTAac-----TATATCCTTTTG TTCCTT (SEQ ID NO: 39 52)

-----249 bp deletion----tgaTATATCCTTTTG TTCCTT (SEQ ID NO: 40 53)

CTCTTTTCCAGACGAGa-----143 bp deletion----- (SEQ ID NO: 41 54)

CTCTTTTCCAGACGAGTA-----188 bp deletion----- (SEQ ID NO: 42 55)

-----463 bp deletion-----

CTCTTTTCCAGACGAGTAattgtttactctcagtcagtcacatgtcgaTATCCTTTTG TTCCTT
(SEQ ID NO: 43 56)
